

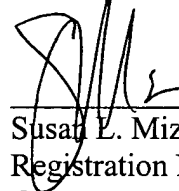
REMARKS

This preliminary amendment is submitted to amended the format of the claims to current U.S. claiming conventions. The Commissioner is hereby authorized to charge any fees or credit any over-payment associated with this communication to Deposit Account No. 50-0902 (75978/10786).

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Respectfully Submitted,

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MARKED-UP VERSION OF PENDING CLAIMS

1. (Canceled) A method of separation of an antibody from a mixture of the antibody and at least one contaminant, the method comprising:
 - (a) placing the antibody and contaminant mixture in a first solvent stream, the first solvent stream being separated from a second solvent stream by an electrophoretic membrane;
 - (b) selecting a pH for the first solvent stream such that contaminants with an isoelectric point (pI) lower than the antibody to be separated will be charged;
 - (c) applying an electric potential between the two solvent streams causing movement of at least some of the contaminants through the membrane into the second solvent stream while the antibody is substantially retained in the first solvent stream, or if entering the membrane, being substantially prevented from entering the second solvent stream;
 - (d) optionally, periodically stopping and reversing the electric potential to cause movement of any antibody having entered the membrane to move back into the first solvent stream, wherein substantially not causing any contaminants that have entered the second solvent stream to re-enter first solvent stream; and
 - (e) repeating step (c) and optionally step (d) until the first solvent stream contains the desired purity of antibody.
2. (Canceled) The method according to claim 1 wherein the antibody and contaminant mixture is a monoclonal antibody in ascitic fluid.
3. (Canceled) The method according to claim 1 or 2 wherein the electrophoretic membrane has a molecular mass cut-off of 50 to 150 kDa.
4. (Canceled) The method according to claim 3 wherein the electrophoretic membrane has a molecular mass cut-off of 100 kDa.
5. (Canceled) The method according to any one of claims 1 to 4 wherein the pH of the first solvent stream is 7.5 to 9.5.

6. (Canceled) The method according to any one of claims 1 to 5 further including the steps of:

- (f) placing the separated antibody in a fresh first solvent stream, the first solvent stream being separated from a second solvent stream by an electrophoretic membrane;
- (g) selecting a pH of the fresh solvent stream such that the pH is within 1 pH unit of the pI of the antibody;
- (h) applying an electric potential between the two solvent streams causing movement of at least some of the contaminants through the membrane into the second solvent stream while the antibody is substantially retained in the fresh first solvent stream, or if entering the membrane, being substantially prevented from entering the second solvent stream;
- (i) optionally, periodically stopping and reversing the electric potential to cause movement of any antibody having entered the membrane to move back into the fresh first solvent stream, wherein substantially not causing any contaminants that have entered the second solvent stream to re-enter fresh first solvent stream; and
- (j) repeating step (h) and optionally step (i) until the fresh first solvent stream contains the desired purity of antibody.

7. (Canceled) The method according to claim 6 wherein the molecular mass cut-off of the membrane used in step (f) is larger than that used in step (b).

8. (Canceled) The method according to claim 7 wherein the molecular mass cut-off of the electrophoretic membrane used in step (f) is at least 200 kDa.

9. (Canceled) The method according to claim 8 wherein the molecular mass cut-off of the electrophoretic membrane used in step (f) is 1000 kDa.

10. (Canceled) The method according to any one of claims 6 to 9 wherein the pH in step (g) is from 6 to 8.

11. (Canceled) The method according any one of claims 6 to 9 wherein the pH in step (g) is within 0.5 pH units of the pI of the antibody.
12. (Canceled) The method according to any one of claims 1 to 11 wherein percent recover of the antibody is at least 70%.
13. (Canceled) The method according to claim 12 wherein percent recovery of the antibody is at least 90%.
14. (Canceled) A method of separation of an antibody from a mixture of the antibody and at least one contaminant, the method comprising:
- (a) placing the separated antibody in a first solvent stream, the first solvent stream being separated from a second solvent stream by an electrophoretic membrane;
 - (b) selecting a pH of the first solvent stream such that the pH is within 1 pH unit of the pI of the antibody;
 - (c) applying an electric potential between the two solvent streams causing movement of at least some of the contaminants through the membrane into the second solvent stream while the antibody is substantially retained in the first solvent stream, or if entering the membrane, being substantially prevented from entering the second solvent stream;
 - (d) optionally, periodically stopping and reversing the electric potential to cause movement of any antibody having entered the membrane to move back into the first solvent stream, wherein substantially not causing any contaminants that have entered the second solvent stream to re-enter first solvent stream; and
 - (e) repeating step (c) and optionally step (d) until the first solvent stream contains the desired purity of antibody.
15. (Canceled) The method according to claim 14 wherein the antibody and contaminant mixture is a monoclonal antibody in ascitic fluid.
16. (Canceled) The method according to claim 14 or 15 wherein the molecular mass cut-off of the electrophoretic membrane used in step (a) is at least 200 kDa.

17. (Canceled) The method according to claim 16 wherein the molecular mass cut-off of the electrophoretic membrane used in step (a) is 1000 kDa.

18. (Canceled) The method according to any one of claims 14 to 17 wherein the pH in step (b) is from 6 to 8.

19. (Canceled) The method according to any one of claims 14 to 17 wherein the pH in step (b) is within 0.5 pH units of the pI of the antibody.

20. (Canceled) An antibody purified by the method according to any one of claims 1 to 19.

21. (Canceled) An antibody purified by the method according to any one of claims 1 to 19.

22. (New) A method for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant, the method comprising:

(a) directing a first fluid stream having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, so as to flow along a first selective membrane, wherein such pH is selected such that contaminants with an isoelectric point lower than the isoelectric point of the at least one antibody will have a net charge;

(b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

(c) applying at least one selected electric potential across at least the first and second fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid stream; and

(d) maintaining step (c) until at least one of the fluid streams contains the desired purity of the at least one antibody.

23. (New) The method according to claim 22 wherein the mixture is comprised of monoclonal antibodies in ascitic fluid.

24. (New) The method according to claim 22 wherein the first selective membrane has a molecular mass cut-off between about 50 kDa to about 150 kDa.

25. (New) The method according to claim 24 wherein the first selective membrane has a molecular mass cut-off of about 100 kDa.

26. (New) The method according to claim 22 wherein the pH of the first fluid stream is between about 7.5 to about 9.5.

27. (New) The method according to claim 22 wherein the method further comprises periodically stopping and reversing the at least one selected electric potential to cause movement of at least any components in the first fluid stream having entered the first selective membrane to move back into the first fluid stream and wherein substantially not causing any components which have entered the second fluid stream to re-enter the first fluid stream.

28. (New) The method according to claim 22 wherein the yield of the at least one antibody is at least about 70%.

29. (New) The method according to claim 22 wherein the yield of the at least one antibody is at least about 90%.

ai 30. (New) The method according to claim 22 wherein the method further comprises
(e) recovering the at least one antibody isolated from the mixture from at least one of the first and second fluid streams;

(f) providing the at least one antibody into a third fluid stream having a selected pH and directing the third fluid stream so as to flow along a second selective membrane, wherein the pH is selected such that it is within about 1 pH unit of the at least one antibody;

(g) directing a fourth fluid stream along the second selective membrane so as to be isolated from the third fluid stream thereby;

(h) applying at least one selected electric potential across at least the third and fourth fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and other components in the third fluid stream through the second selective membrane while at least a portion of the other of the at least one antibody and other components in the third fluid stream is prevented from entering the second fluid stream; and

(i) maintaining step (h) until at least one of the fluid streams contains the desired purity of the at least one antibody.

31. (New) The method according to claim 30 wherein the second selective membrane has a larger molecular mass cut-off than the first selective membrane.

32. (New) The method according to claim 30 wherein the molecular mass cut-off of the second selective membrane is at least about 200 kDa.

33. (New) The method according to claim 30 wherein the molecular mass cut-off of the second selective membrane is about 1000 kDa.

34. (New) The method according to claim 30 wherein the pH of the third fluid stream is from about 6 to about 8.

35. (New) The method according to claim 30 wherein the pH of the third fluid stream is within 0.5 pH units of the at least one antibody.

36. (New) The method according to claim 30 wherein the yield of the at least one antibody is at least about 70%.

37. (New) The method according to claim 30 wherein the yield of the at least one antibody is at least about 90%.

38. (New) The method according to claim 30 wherein the method further comprises periodically stopping and reversing the at least one selected electric potential to cause movement of at least any components in the third fluid stream having entered the second selective membrane to move back into the third fluid stream and wherein substantially not causing any components which have entered the fourth fluid stream to re-enter the third fluid stream.

39. (New) A method for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant comprising:

(a) directing a first fluid stream having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, so as to flow along a first selective membrane, wherein such pH is that it is within about 1 pH unit of the at least one antibody;

(b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

(c) applying at least one selected electric potential across at least the first and second fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid stream; and

(d) maintaining step (c) until at least one of the fluid streams contains the desired purity of the at least one antibody.

40. (New) The method according to claim 39 wherein the mixture is comprised of monoclonal antibodies in ascitic fluid.

41. (New) The method according to claim 39 wherein the molecular mass cut-off of the first selective membrane is at least about 200 kDa.

42. (New) The method according to claim 39 wherein the molecular mass cut-off of the first selective membrane is about 1000 kDa.

43. (New) The method according to claim 39 wherein the pH of the first fluid stream is from about 6 to about 8.

44. (New) The method according to claim 39 wherein the pH of the first fluid stream is within 0.5 pH units of the at least one antibody.

45. (New) The method according to claim 39 wherein the yield of the at least one antibody is at least about 70%.

46. (New) The method according to claim 39 wherein the yield of the at least one antibody is at least about 90%.

47. (New) The method according to claim 39 wherein the method further comprises periodically stopping and reversing the at least one selected electric potential to cause movement of at least any components in the third fluid stream having entered the second selective membrane to move back into the third fluid stream and wherein substantially not causing any components which have entered the fourth fluid stream to re-enter the third fluid stream.

48. (New) A system for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant comprising:

means adapted for directing a first fluid stream having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, so as to flow along a first selective membrane, wherein such pH is selected such that contaminants with an isoelectric point lower than the isoelectric point of the at least one antibody will have a net charge;

means adapted for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby; and

means adapted for applying at least one selected electric potential across at least the first and second fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid stream.

49. (New) The system according to claim 48 wherein the system further comprises:

means adapted for recovering the at least one antibody isolated from the mixture from at least one of the first and second fluid streams;

means adapted for providing the at least one antibody into a third fluid stream having a selected pH and directing the third fluid stream so as to flow along a second selective membrane, wherein the pH is selected such that it is within about 1 pH unit of the at least one antibody;

means adapted for directing a fourth fluid stream along the second selective membrane so as to be isolated from the third fluid stream thereby; and

means adapted for applying at least one selected electric potential across at least the third and fourth fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and other components in the third fluid stream through the second selective membrane while at least a portion of the other of the at least one antibody and other components in the third fluid stream is prevented from entering the second fluid stream.

50. (New) A system for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant comprising:

means adapted for directing a first fluid stream having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, so as to flow along a first selective membrane, wherein such pH is that it is within about 1 pH unit of the at least one antibody;

means adapted for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby; and

means adapted for applying at least one selected electric potential across at least the first and second fluid streams, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid stream.

51. (New) A method for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant, the method comprising:

(a) communicating a first fluid volume having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, along a first selective membrane, wherein such pH is selected such that contaminants with an isoelectric point lower than the isoelectric point of the at least one antibody will have a net charge;

(b) communicating a second fluid volume along the first selective membrane so as to be isolated from the first fluid volume thereby;

(c) applying at least one selected electric potential across at least the first and second fluid volumes, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid volume; and

(d) maintaining step (c) until at least one of the fluid volumes contains the desired purity of the at least one antibody.

52. (New) A method for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant comprising:

(a) communicating a first fluid volume having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, along a first selective membrane, wherein such pH is that it is within about 1 pH unit of the at least one antibody;

(b) communicating a second fluid volume along the first selective membrane so as to be isolated from the first fluid volume thereby;

(c) applying at least one selected electric potential across at least the first and second fluid volumes, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid volume; and

(d) maintaining step (c) until at least one of the fluid volumes contains the desired purity of the at least one antibody.

53. (New) A system for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant, the method comprising:

means adapted for communicating a first fluid volume having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, along a first selective membrane, wherein such pH is selected such that contaminants with an isoelectric point lower than the isoelectric point of the at least one antibody will have a net charge;

means adapted for communicating a second fluid volume along the first selective membrane so as to be isolated from the first fluid volume thereby; and

means adapted for applying at least one selected electric potential across at least the first and second fluid volumes, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid volume one of the fluid volumes contains the desired purity of the at least one antibody.

54. (New) A system for isolating at least one antibody from a mixture containing the at least one antibody and at least one contaminant comprising:

means adapted for communicating a first fluid volume having a selected pH and including the mixture containing at least one antibody and the at least one contaminant, along a

first selective membrane, wherein such pH is that it is within about 1 pH unit of the at least one antibody;

means adapted for communicating a second fluid volume along the first selective membrane so as to be isolated from the first fluid volume thereby; and

means adapted for applying at least one selected electric potential across at least the first and second fluid volumes, wherein the application of the at least one selected electric potential causes migration of at least a portion of a selected one of the at least one antibody and the at least one contaminant through the first selective membrane while at least a portion of the other of the at least one antibody and the at least one contaminant is prevented from entering the second fluid volume.

55. (New) An antibody purified by the method according to claim 22.

56. (New) The antibody according to claim 55 wherein the antibody is a monoclonal antibody.

57. (New) An antibody purified by the method according to claim 30.

58. (New) The antibody according to claim 57 wherein the antibody is a monoclonal antibody.

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